# PATENT COOPERATION TREATY

# PCT

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44*bis*)

| | | |
|---|---|---|
| Applicant's or agent's file reference<br>042881-0207 | **FOR FURTHER ACTION** | See item 4 below |
| International application No.<br>PCT/IB2005/002479 | International filing date *(day/month/year)*<br>01 April 2005 (01.04.2005) | Priority date *(day/month/year)*<br>01 April 2004 (01.04.2004) |
| International Patent Classification (8th edition unless older edition indicated)<br>See relevant information in Form PCT/ISA/237 | | |
| Applicant<br>BIOMIRA, INC. | | |

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 *bis*.1(a).

2. This REPORT consists of a total of 8 sheets, including this cover sheet.

   In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

| | | |
|---|---|---|
| ☒ | Box No. I | Basis of the report |
| ☒ | Box No. II | Priority |
| ☒ | Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability |
| ☐ | Box No. IV | Lack of unity of invention |
| ☒ | Box No. V | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| ☐ | Box No. VI | Certain documents cited |
| ☐ | Box No. VII | Certain defects in the international application |
| ☒ | Box No. VIII | Certain observations on the international application |

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44*bis*.3(c) and 93*bis*.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44*bis* .2).

| | |
|---|---|
| | Date of issuance of this report<br>04 October 2006 (04.10.2006) |
| The International Bureau of WIPO<br>34, chemin des Colombettes<br>1211 Geneva 20, Switzerland<br>Facsimile No. +41 22 338 82 70 | Authorized officer<br>Cecile Chatel<br>e-mail: pt13@wipo.int |

Form PCT/IB/373 (January 2004)

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY



PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

To:
SIMKIN, MICHELE M.
c/o FOLEY & LARDNER LLP
Washington Harbour
3000 K Street, N.W.
Suite 500
Washington, District of Columbia
United States, 20007

Date of mailing *(day/month/year)* 27 January 2006 (27-01-2006)

Applicant's or agent's file reference
042881-0207

**FOR FURTHER ACTION**
See paragraph 2 below

| International application No. | International filing date *(day/month/year)* | Priority date *(day/month/year)* |
|---|---|---|
| **PCT/IB2005/002479** | 01 April 2005 (01-04-2005) | 01 April 2004 (01-04-2004) |

International Patent Classification (IPC) or both national classification and IPC
IPC: ***A61K 39/00*** (2006.01) , ***A61P 35/00*** (2006.01) , ***A61K 38/17*** (2006.01)

Applicant
BIOMIRA INC. ET AL

1. This opinion contains indications relating to the following items :

| | | |
|---|---|---|
| [X] | Box No. I | Basis of the opinion |
| [X] | Box No. II | Priority |
| [X] | Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability |
| [ ] | Box No. IV | Lack of unity of invention |
| [X] | Box No. V | Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| [ ] | Box No. VI | Certain documents cited |
| [ ] | Box No. VII | Certain defects in the international application |
| [X] | Box No. VIII | Certain observations on the international application |

2. **FURTHER ACTION**
If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

| Name and mailing address of the ISA/CA | Date of completion of this opinion | Authorized officer |
|---|---|---|
| Canadian Intellectual Property Office<br>Place du Portage I, C114 - 1st Floor, Box PCT<br>50 Victoria Street<br>Gatineau, Quebec K1A 0C9<br>Facsimile No.: 001(819)953-2476 | 9 January 2006 (09-01-2006) | Qianfa Chen (819) 994-1374 |

**Box No. I Basis of this opinion**

1. With regard to the **language**, this opinion has been established on the basis of:

   [X] the international application in the language in which it was filed

   [ ] a translation of the international application into , which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of :

   a. type of material

      [X] a sequence listing

      [ ] table(s) related to the sequence listing

   b. format of material

      [X] on paper

      [X] in electronic form

   c. time of filing/furnishing

      [ ] contained in the international application as filed.

      [ ] filed together with the international application in electronic form

      [X] furnished subsequently to this Authority for the purposes of search.

3 [ ] In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statement that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments :

**Box No. II Priority**

1. [X] The validity of the priority claim has not been considered because the International Searching Authority does not have in its possession a copy of the earlier application whose priority has been claimed or, where required, a translation of that earlier application. This opinion has nevertheless been established on the assumption that the relevant date (Rules 43bis.1 and 64.1) is the claimed priority date.

2. [ ] This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary :

**Box No. III** **Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of :

[ ] the entire international application

[X] claim Nos. 1-30

because:

[X] the said international application, or the said claim Nos. 1-30 relate to the following subject matter which does not require an international search *(specify)* :

Claims 1-30, directed to a method for treatment of the human or animal body by surgery or therapy, are not required to be searched nor is a written opinion required by this Authority under Rule 67.1(iv) of the PCT. Regardless, this Authority has established a written opinion based on the alleged effect(s) or purpose(s)/use(s) of the product defined in claims 1-30.

[ ] the description, claims or drawings *(indicate particular elements below)* or said claim Nos. are so unclear that no meaningful opinion could be formed *(specify)* :

[ ] the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed *(specify):*

[ ] no international search report has been established for said claims Nos.

[ ] a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

[ ] furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.

[ ] furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.

[ ] pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rule 13*ter*.1(a) or (b).

[ ] a meaningful opinion could not be formed without the tables related to the sequence listings; the applicant did not, within the prescribed time limit, furnish such tables in electronic form complying with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions, and such tables were not available to the International Searching Authority in a form and manner acceptable to it.

[ ] the tables related to the nucleotide and/or amino acid sequence listing, if in electronic form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

[ ] See Supplemental Box for further details.

**Box No. V** **Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

| | | | |
|---|---|---|---|
| Novelty (N) | Claims | 2 and 19 | YES |
| | Claims | 1,3-18 and 20-30 | NO |
| Inventive step (IS) | Claims | | YES |
| | Claims | 1-30 | NO |
| Industrial applicability (IA) | Claims | 1-30 | YES |
| | Claims | | NO |

2. Citations and explanations :

Reference is made to the following documents:

D1: MORSE, M.A. Technology evaluation: BLP-25, Biomira Inc. Curr. Opin. Mol. Ther. February 2001, Vol.3, No.1, Pages 102-105, ISSN: 1464-8431.
See the entire document

D2: US 2002/0051813 A1 (BONI, L. et al.), 2 May 2002
See paragraphs 0039, 0043 and 0044.

D3: WO 02/43699 A2 (BONI, L. et al.), 6 June 2002
See Page 8, line 25 to page 9, line 27.

D4: SCHUT, I.C. et al. MUC1 expression, splice variant and short form transcription (MUC1/Z, MUC1/Y) in prostate cell lines and tissue. BJU International, February 2003, Vol. 91, No.3, Pages 278-283, ISSN: 1464-4096.
See abstract.

D1 describes a method for treating an individual having various cancers such as non-small cell lung cancer (NSCLC) with a liposomal formulation comprising a MUC-1 peptide-based vaccine, wherein the formulation comprises a 25-amino acid MUC-1 peptide (BLP-25) and adjuvant (monophosphoryl lipid A). In a phase I study of 16 patients with either stage IIIb or IV NSCLC, a single dose of cyclophosphamide was given to inhibit suppressor T-cell function. The patients received 20-200 µg of BLP-25 subcutaneously on weeks 0, 2, 5 and 9. In a phase II trial of BLP-25 in patients with advanced NSCLC, higher or more frequent dosing of BLP-25 in combination with cytokine IL-2 was administered. The evaluation of the treated patients comprises measuring the induction of immune response such as a T-cell response against MUC-1, the eradication of tumour, and the survival of the treated patients. The amino acid sequence of BLP-25 of D1 is identical to the amino acid sequence of SEQ ID NO: 1 of the instant international application.

D2 and D3 separately describe a method for the delivery of an anti-tumour vaccine which comprises liposomes containing a synthetic MUC-1 peptide (a preferred tumour antigen), monophosphoyl Lipid A, and/or IL2. Many human adenocarcinomas, such as breast, colon, lung, ovarian and pancreatic cancers, abundantly overexpress and secrete underglycosylated MUC-1 protein. A high level of MUC-1 expression is associated with a high metastatic potential and poor prognosis. MUC-1 is, therefore, a clinically significant marker of these cancers. A preferred

[Continuation in Supplemental Box]

**Box No. VIII Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made :

D. Description Defects

The description does not comply with Article 5 of the PCT. A statement in an application, such as found on page 1, line 6, page 31, line 17, which incorporates by reference any other document, does not comply with Article 5 PCT. The description should be complete in and of itself. A person skilled in the art should be able to understand the patent specification without reference to any other document.

E. Claim Defects

Claims 1 and 2 do not comply with Article 6 of the PCT. Referring to a polypeptide by the expression "a variant of" an amino acid sequence without defining the nature of the variation is meaningless.

Claims 12 and 30 are ambiguous, when they depend on claim 2, and do not comply with Article 6 of the PCT. According to the description, the claimed stages of cancers in claims 12 and 30 relate to lung cancer not prostate cancer.

Claim 16 does not comply with Article 6 of the PCT. The claim is ambiguous in that the Markush set elements are listed in the alternative (i.e., or) rather than collective (i.e., and).

In claim 22, "MUC-1" should probably read "MUC-1 peptide".

**Supplemental Box**

In case **the space in any of the preceding boxes is not sufficient.**

Continuation of:

MUC-1 peptide is BP1-148 (27 amino acids) with a palmitoyl group at the epsilon amino group of the C-terminal lysine. The amino acid sequence of BP1-148 of D2 or D3 is identical to the amino acid sequence of SEQ ID NO: 2 of the instant international application.

D4 describes that benign prostatic hyperplasia, prostate cancer and metastatic prostate cancer all express high levels of underglycosylated MUC-1.

A. Novelty

Claims 1, 18 and their dependent claims 3-17 and 20-30 when they relate to SEQ ID NO. 1 and non-small cell lung cancer (NSCLC), lack novelty and do not comply with Article 33(2) of the PCT, as being anticipated by D1 which describes a method for treating an individual having various cancers such as NSCLC with a liposomal formulation of MUC-1 peptide-based vaccine, wherein the formulation comprises a 25-amino acid MUC-1 peptide (BLP-25) and adjuvant (monophosphoryl lipid A). The amino acid sequence of BLP-25 of D1 is identical to the amino acid sequence of SEQ ID NO: 1 of the instant international application.

Claims 1, 18 and their dependent claims 3-17 and 20-30 when they relate to SEQ ID NO. 2 and NSCLC, lack novelty and do not comply with Article 33(2) of the PCT, as being anticipated by D2 or D3. D2 or D3 separately describe a method for the delivery of an anti-lung cancer vaccine which comprises liposomes containing a synthetic MUC-1 peptide (BP1-148) and monophosphoyl Lipid A. The amino acid sequence of BP1-148 of D2 or D3 is identical to the amino acid sequence of SEQ ID NO: 2 of the current international application.

B. Inventive Steps

Claims 2, 19 and their dependent claims 3-17 and 20-30 when they relate to SEQ ID NOs: 1 or 2 and prostate cancer, do not comply with Article 33(3) of the PCT. The subject matter of these claims would have been obvious on the claim date to a person skilled in the art or science to which it pertains having regard D1, D2 or D3 in combination with D4. D1, D2 or D3 separately describe a method for the delivery of an anti-tumour vaccine which comprises liposomes containing a synthetic MUC-1 peptide (e.g., BLP-25 in D1 and BP1-148 in D2 or D3) and monophosphoyl Lipid A. The anti-tumour vaccine can be used to treat various cancers based on the fact that many human adenocarcinomas, such as breast, colon, lung, ovarian and pancreatic cancers, abundantly overexpress and secrete underglycosylated MUC-1 protein. D1, D2 or D3 does not describe the MUC-1 vaccine (BLP-25 or BP1-148) for treating prostate cancer. However, D4 describes that benign prostatic hyperplasia, prostate cancer and metastatic prostate cancer all express high levels of underglycosylated MUC-1 as compared to normal cells, analogous to expression levels of secreted underglycosylated MUC-1 protein in other cancers. Therefore, it would be obvious to a person skilled in the art to follow the teachings of D4 to use the MUC-1 vaccine (BLP-25) of D1 or the MUC-1 vaccine (BP1-148) of D2 or D3 for treating the prostate cancer of D4 thereby arriving at the subject matter of claims 2, 19 and the claims dependent thereon.

C. Industrial Applicability

Claims 1-30 have industrial applicability as defined under Article 33(4) of the PCT.